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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,862	06/24/2003	Kenneth Walter Locke	215233-00500	7180
27160	7590	06/02/2005	EXAMINER	
KATTEN MUCHIN ROSENMAN LLP			OH, TAYLOR V	
525 WEST MONROE STREET			ART UNIT	
CHICAGO, IL 60661-3693			PAPER NUMBER	
			1625	

DATE MAILED: 06/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/601,862

Applicant(s)

LOCKE ET AL.

Examiner

Taylor Victor Oh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 February 2005.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-9 and 11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-9 and 11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 June 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date. _____ | 6) <input type="checkbox"/> Other: _____ |

Final Rejection

The Status of Claims

Claims 1-3, 5-9, and 11 are pending.

Claims 1-3, 5-9, and 11 have been rejected.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, has been maintained due to applicants' failure to modify the claims in the amendment.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of Claims 4, 10, and 12 under 35 U.S.C. 112, second paragraph, has been withdrawn due to the cancellation of the claims in the amendment.

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However, the rejection of claims 1-3, 5-9, and 11 has been maintained due to applicants' failure to modify the claims in the amendment.

Claims 5 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 5 and 11, the phrase "polymorphic forms B and C about $9^{\circ} 2\text{-theta}$ " is recited. This expression is vague and indefinite. The specific PXRD patterns of polymorphic forms B and C are needed to identify each of the specific crystalline Forms B and C which are uniquely different from the other polymorphic form by reciting their corresponding X-ray diffraction values because the x-ray pattern of a pure crystalline substance can be considered as a "fingerprint" with each crystalline material having within limits, a unique diffraction pattern; furthermore, there are other characteristics to be used in order to distinguish each of the polymorphic Forms B and C further from the other polymorphic forms, such as bioavailability, solubility, dissolution rate, chemical and physical stability, melting point, color, filterability, density, and flow properties. In addition, the polymorphs are further characterized by other analytical techniques such as differential scanning calorimetry, hot stage optical microscopy, and Raman and infrared spectroscopy. The above techniques are essential tools to be used for identifying each of the "polymorphic Forms B and C" clearly; and it is up to applicants to select which critical parameters may be used so as to establish the unique "polymorphic Forms B and C."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of Claims 1-2, 5, 8-9, and 11 under 35 U.S.C. 102(b) as being anticipated clearly by Ohashi et al (U.S. 4,985, 585) .

The rejection of Claims 1-2, 5, 8-9, and 11 under 35 U.S.C. 102(b) as being anticipated clearly by Ohashi et al (U.S. 4,985, 585) has been maintained for the reasons of the record on 8/11/04.

Claim Rejections-35 USC 103

1. Applicants' argument filed 2/25/05 have been fully considered but they are not persuasive.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection of Claims 1-3, 5-9, and 11 under 35 U.S.C. 103(a) as being unpatentable over Ohashi et al (U.S. 4,985, 585) in view of Grant et al (Grant & Hack's Chemical Dictionary , 1990 , p. 328) .

The rejection of Claims 1-3, 5-9, and 11 under 35 U.S.C. 103(a) as being unpatentable over Ohashi et al (U.S. 4,985, 585) in view of Grant et al (Grant & Hack's Chemical Dictionary , 1990 , p. 328) has been maintained for the reasons of the record on 8/11/04.

Applicants' Argument

2. Applicants argue the following issues:
 1. Since a PXRD spectrum may be considered a fingerprint of the desired compound, Figure 6 of the specification containing the fingerprints of form A, B, C allows the skilled artisan in the art to readily identify these different crystal products using PXRD analysis;
 2. There is no change in polymorphic form occurred by placing form A in a

tablet as shown in OA page 3 , lines 8-9 and there is no solubility test for the mixtures of form A and form B, but a solubility test for each form, therefore, the polymorphic form is enabled;

3. Nothing in Ohashi et al suggest the possibility that the crystals can have three different polymorphic forms.

Applicants' arguments have been noted, but the arguments are not persuasive.

First, regarding the first applicant's argument, the Examiner has noted applicants' argument. However, in claims 5 and 11, each of the polymorphic forms A, B, and C are clearly not identified because there are no their corresponding X-ray diffraction values for each of them in the claims; this does lead to the ambiguity of the claims as a whole.

Moreover, the second paragraph of 35 USC 112 requires that the claims particularly point out the subject matter that applicants regard as the invention. A claim referring to the specification is improper. Exparte Fressola, 27 U.S.P.Q. 2d 1608 (U.S. Pat. & Trademark Bd. Pat. App. & Int 1993).

Therefore, the rejection under second paragraph of 35 USC 112 is still applicable to the claimed invention.

Second, regarding the second applicant's arguments, the Examiner has noted applicants' argument. However, the claims 1-3, and 5-7 are directed to a pharmaceutical composition comprising the polymorphic various forms of 4-(6-acetyl-3-

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(3-(4-acetyl-3-hydroxy-2-propylphenylthio)propoxy)-2-propylphenoxy)butyric acid.

According to the specification, there are some remarks about various polymorphic forms of the 4-(6-acetyl-3-(3-(4-acetyl-3-hydroxy-2-propylphenylthio)propoxy)-2-propylphenoxy)butyric acid, but there are no other information about which polymorphic form in the pharmaceutical composition is effective regarding its bioavailability as well as there is no information about the X-ray pattern for Form A in the tablet or capsule in the specification. It is not uncommon to find several polymorphs of compounds existing under normal handling conditions. Every polymorph has its own characteristic X-ray patterns during the pharmaceutical process of making even the final forms such as tablet or capsule containing the active ingredient.

Furthermore, many different polymorphs and /or solvates show varying dissolution rates under different conditions : humidity, pressure, temperature, and etc.. Therefore, on the time scale of the pharmaceutical bioavailability, different total amounts of drug are dissolved, resulting in potential bio-inequivalence of the several forms of the drug. Since the above essential aspects are absent in the specification, the skilled artisan in the art is unable to determine which polymorphic form of 4-(6-acetyl-3-(3-(4-acetyl-3-hydroxy-2-propylphenylthio)propoxy)-2-propylphenoxy)butyric acid is suitable for the pharmaceutical composition with respect to the pharmaceutical bioavailability and the absence of the unique characteristic X-ray pattern for form X in the tablet and capsule form. Therefore, applicants' arguments are not persuasive.

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Third, regarding the third applicant's arguments, the Examiner has noted applicants' argument. However, each of the polymorphic forms A, B, and C are clearly not identified because there are no their corresponding X-ray diffraction values for each of them in the claims; this does lead to the ambiguity of the claims as a whole. Furthermore, it is known in the art that it is not uncommon to find several polymorphs of compounds existing under normal handling conditions; therefore, Ohashi's et al compound does inherently have different polymorphs. Thus, the prior art is still relevant to the rejection of the claimed invention.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Taylor Victor Oh
5/28/05

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